REMARKS

Status of the Claims

Claims 1, 3 to 9, 21, 22 and 25 to 27 were pending. Claim 1 has been amended as shown above to make explicit that the transducer and intracellular enzymatic signal converting domain are separate molecules. *See, e.g.,* Figure 2 of the as-filed specification. In addition, the limitations of previous claims 7 and 8 have been incorporated into claim 1. As no new matter has been added and as arguments regarding this now explicit distinction of the claimed elements have been considered, entry of the amendment after final is in order. Thus, claims 1, 3-6, 9, 21, 22 and 25 to 27 are pending as shown above.

35 U.S.C. §103

Claims 1, 3-9, 21, 22 and 27 were again rejected under 35 U.S.C. § 103(a) as obvious over U.S. Patent No. 5,521,066 (hereinafter "Menzel") in view of U.S. Patent No. 5,348,867 (hereinafter "Georgiou"). (Final Office Action, pages 2-7). Menzel was again cited for disclosing a transmembrane fusion protein comprising a ligand binding domain, a cytoplasmic toxR NDA binding region, a hydrophobic ToxR transmembrane region and a reporter gene operably linked to the ctx operon. *Id.* Menzel was further alleged to disclose that binding a ligand to the ligand binding domain induces a conformational change in the cytoplasmic domain, which in turn induces binding to the promoter region of the reporter gene. *Id.*

The claims have been amended to make explicit what was previously implicit (and argued by Applicants), namely that the claimed transducer and intracellular enzymatic signal transforming domain elements are separate molecules. As repeatedly acknowledged, Menzel's intracellular domain of the transmembrane fusion protein acts directly on the reporter gene promoter – there is no separate transducer as plainly required by the claims. Because a transducer component separate from the intracellular domain molecule is entirely lacking in the system described by Menzel (which relies solely on dimerization of toxR with no transducer whatsoever), Menzel does not teach or suggest all the elements of the claims.

The secondary reference of Georgiou fails to make up for the deficiencies of Menzel. In particular, Georgiou fails to describe or suggest any intracellular enzymatic signal domain for transducing a signal to a transcription activation element. Thus, neither Georgiou nor Menzel, alone or in combination, describe or suggest a recited element of the claims.

For the reasons of record, Menzel and Georgiou do not teach or suggest the claimed elements. There is nothing whatsoever in either reference about ligand-binding domains and transducers as claimed and, accordingly, no combination of Menzel and Georgiou that would result in the claimed biodetectors. Thus, the rejection should be withdrawn.

35 U.S.C. § 112, 1st paragraph, written description

Claims 1, 3-9, 21-22 and 25-27 were again rejected under 35 U.S.C. § 112, 1st paragraph as allegedly not adequately described by the as-filed specification. (Final Office Action, pages 7-10). In particular, it was alleged that the claims encompass "limitless combination of transmembrane fusion proteins" and that only the exemplified biodetectors are described. *See,* Final Office Action, page 8, also stating that "the nucleic acid itself is required."

Applicants again strongly traverse the rejection and supporting remarks

The written description requirement is satisfied when the as-filed specification, in light of the knowledge possessed by the skilled artisan at the time of filing, reasonably conveys that Applicants were in possession of the claimed subject matter, in this case a biodetector including an extracellular antibody domain, an intracellular enzymatic domain, a transducer and a reporter gene. *See, e.g., In re Lukach*, 169 USPQ 795, 796 (CCPA 1971); *In re Lange*, 209 USPQ 288 (CCPA 1981).

The Examiner's assertion that the claims encompass "limitless" combinations of transmembrane fusion proteins is in error. In fact, the claims only encompass transmembrane fusion proteins in which binding of a ligand to the extra-cellular domain converts the intracellular domain to an active form. Similarly, the claims only encompass membrane intracellular domains of the recited types, which were, at the time of filing, well known to specifically able to activate a transducer protein. PhoQ (intracellular enzymatic domain) and PhoP (transducer activated by PhoQ) are but one example provided in the specification. *See,* Example 2, page 27, for additional examples of antibody-phosphatase fusion proteins. The

skilled artisan would be aware that any of the recited systems that can be used interchangeably with PhoQ and PhoP.

It is axiomatic that a specification does not need to re-describe what is well known and based on the ample disclosure in the specification, the skilled artisan would clearly recognize that Applicants were in possession of the claimed biodetectors and withdrawal of the rejection is in order.

CONCLUSION

Applicants respectfully submit that the claims in condition for allowance.

If the Examiner notes any further matters that the Examiner believes may be expedited by a telephone interview, the Examiner is requested to contact the undersigned.

Respectfully submitted,

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